AMENDMENTS TO THE CLAIMS

Claims 20-28 and 41-49 are withdrawn from consideration as related to nonelected subject matter. Please cancel claims 2, 16, and 37. Please amend claims 1, 17, 29, and 33-35.

1. (currently amended) A method of ~~treating, preventing,~~ treating or ameliorating a symptom of multiple sclerosis associated with an IL-10 ~~deficiency,~~ deficiency or increased IFN-γ~~, increased IL-1α, increased IL-2, increased IL-6, or increased IL-18~~ in a subject, the method comprising:

administering to the subject an agonist of an interleukin-21 (IL-21)/IL-21 receptor (IL-21R) in an amount sufficient to ~~treat, prevent,~~ treat or ameliorate the symptom of multiple sclerosis associated with an IL-10 ~~deficiency,~~ deficiency or increased IFN-γ~~, increased IL-1α, increased IL-2, increased IL-6, or increased IL-18,~~ wherein said agonist is selected from the group consisting of an IL-21 polypeptide, an agonistic anti-IL-21R antibody and an antigen-binding fragment of an agonistic anti-IL-21R antibody.

2. (canceled)

3. (original) The method of claim 1, wherein the agonist is an IL-21 polypeptide that comprises a sequence at least 95% identical to the amino acid sequence of SEQ ID NO:2 and is capable of binding to an IL-21R.

4. (original) The method of claim 1, wherein the agonist is an IL-21 polypeptide that comprises the amino acid sequence of SEQ ID NO:2.

5. (previously presented) The method of claim 1, wherein the agonist is an agonistic anti-IL-21R antibody or an antigen-binding fragment thereof.

6. (previously presented) The method of claim 5, wherein the agonistic anti-IL-21R antibody is a human antibody.

7. (original) The method of claim 1, further comprising administering to the subject at least one anti-inflammatory agent.

8. (previously presented) The method of claim 7, wherein the anti-inflammatory agent is selected from the group consisting of IFNβ-1α and IFNβ-1β.

9. (original) The method of claim 1, wherein the subject is a mammal.

10. (original) The method of claim 1, wherein the IL-21/IL-21R agonist is administered in the form of a single dose.

11. (original) The method of claim 1, wherein the IL-21/IL-21R agonist is administered as a series of doses separated by intervals of days, weeks or months.

12. (original) The method of claim 1, wherein the IL-21/IL-21R agonist is administered by injection.

13. (original) The method of claim 12, wherein the IL-21/IL-21R agonist is injected into the central nervous system.

14. (previously presented) The method of claim 12, wherein the IL-21/IL-21R agonist is injected intrathecally or intravenously.

15. (original) The method of claim 12, wherein the IL-21/IL-21R agonist is injected into the lumbar cerebrospinal fluid.

16. (canceled)

17. (currently amended) The method of claim 1, further comprising, prior to the administering:

(a) evaluating an IL-10 parameter of the subject; and

(b) comparing the IL-10 parameter in the subject to an IL-10 parameter of a normal subject known not to have multiple sclerosis, wherein a decrease in the IL-10 parameter in the subject relative to the normal subject indicates that the subject requires ~~treatment, prevention,~~ treatment or amelioration of a symptom of multiple sclerosis associated with an IL-10 deficiency.

18. (previously presented) The method of claim 17, further comprising, after the administering, evaluating an IL-10 parameter of the subject, wherein an increase in the IL-10 parameter indicates a therapeutic effect.

19. (previously presented) The method of claim 1, further comprising, after the administering, evaluating an IL-10 parameter of the subject.

20. (withdrawn) A pharmaceutical composition comprising an IL-21/IL-21R agonist and an anti-inflammatory agent, wherein said IL-21/IL-21R agonist is selected from the group consisting of an IL-21 polypeptide, an agonistic anti-IL21R antibody and an antigen-binding fragment of an agonistic anti-IL21R antibody.

21. (withdrawn) The pharmaceutical composition of claim 20, wherein the IL-21 polypeptide has a sequence at least 90% identical to the amino acid sequence of SEQ ID NO:2 and is capable of binding to an IL-21R.

22. (withdrawn) The pharmaceutical composition of claim 20, wherein the IL-21 polypeptide has a sequence at least 95% identical to the amino acid sequence of SEQ ID NO:2 and is capable of binding to an IL-21R.

23. (withdrawn) The pharmaceutical composition of claim 20, wherein said IL-21/IL-21R agonist comprises the amino acid sequence of SEQ ID NO:2.

24. (withdrawn) The pharmaceutical composition of claim 20, wherein the anti-inflammatory agent is selected from the group consisting of IFN β -1α, IFNβ -1β, TNF antagonists, IL-12 antagonists, IL-23 antagonists, methotrexate, leflunomide, sirolimus (rapamycin), and CCI-779.

25. (withdrawn) The pharmaceutical composition of claim 20, wherein the agonist is an agonistic anti-IL21R antibody or an antigen-binding fragment thereof.

26. (withdrawn) The pharmaceutical composition of claim 25, wherein the agonistic anti-IL21R antibody is a human antibody.

27. (withdrawn) A pharmaceutical composition comprising an IL-21/IL-21R agonist and a protein that simulates myelin basic protein, wherein said IL-21/IL-21R agonist is selected from the group consisting of an IL-21 polypeptide, an agonistic anti-IL21R antibody and an antigen-binding fragment of an agonistic anti-IL21R antibody.

28. (withdrawn) The pharmaceutical composition of claim 27 wherein the IL-21/IL-21R agonist is a protein that comprises an IL-21 polypeptide, and the protein that simulates myelin basic protein comprises glatiramer acetate.

29. (currently amended) A method of ~~treating, preventing,~~ treating or ameliorating multiple sclerosis associated with an IL-10 ~~deficiency,~~ deficiency or increased IFN-γ, ~~increased~~

~~IL-1α, increased IL-2, increased IL-6, or increased IL-18,~~ in a mammalian subject, the method comprising:

administering to the subject an agonistic interleukin-21 (IL-21) polypeptide in an amount sufficient to ~~treat, prevent,~~ treat or ameliorate multiple sclerosis associated with an IL-10 ~~deficiency,~~ deficiency or increased IFN-γ~~, increased IL-1α, increased IL-2, increased IL-6, or increased IL-18,~~ or at least one symptom of multiple sclerosis associated with an IL-10 ~~deficiency,~~ deficiency or increased IFN-γ, ~~increased IL-1α, increased IL-2, increased IL-6, or increased IL-18,~~ in the subject.

30. (original) The method of claim 29 wherein the subject is human, and the IL-21 polypeptide is a human IL-21 polypeptide.

31. (original) The method of claim 30 wherein the IL-21 polypeptide comprises SEQ ID NO:2.

32. (original) The method of claim 30 wherein the IL-21 polypeptide is recombinantly produced.

33. (currently amended) The method of claim 32~~30~~ wherein the IL-21 polypeptide is recombinantly produced in a bacterial cell.

34. (currently amended) A method of ~~treating, preventing,~~ treating or ameliorating an IL-10 deficiency, or a disorder associated with an IL-10 deficiency in a mammalian subject, the method comprising:

administering to the subject an agonistic interleukin-21 (IL-21) polypeptide in an amount sufficient to increase IL-10 expression ~~or activity~~ in the subject.

35. (currently amended) A method of ~~treating, preventing,~~ treating or ameliorating an immunological disorder associated with an IL-10 deficiency in a mammalian subject, the method comprising:

(a) evaluating an IL-10 parameter in a mammalian subject;

(b) comparing the IL-10 parameter in the mammalian subject to an IL-10 parameter in a normal mammalian subject known not to have an immunological disorder associated with an IL-10 deficiency, wherein a decrease in the IL-10 parameter in the mammalian subject relative to the normal mammalian subject indicates that the mammalian subject requires treatment~~, prevention,~~ or amelioration of an immunological disorder associated with an IL-10 deficiency; and

(c) administering, to the mammalian subject, an agonistic interleukin-21 (IL-21) polypeptide in an amount that is dependent on the results of comparing step (b).

36. (original) The method of claim 35 wherein the IL-10 parameter comprises quantitative information about levels of IL-10 protein or IL-10 mRNA.

37. (canceled)

38. (original) The method of claim 35 wherein the immunological disorder is a neurological disorder.

39. (original) The method of claim 38 wherein the subject is human and the immunological disorder is multiple sclerosis.

40. (previously presented) The method of claim 38 wherein the immunological disorder is characterized by damage, degradation, or loss of myelin sheaths.

41. (withdrawn) A method of evaluating treatment of multiple sclerosis in a mammalian subject, the method comprising:

administering, to the subject, an agonist of an interleukin-21 (IL-21)/IL-21 receptor (IL-21R); and

evaluating an IL-10 parameter in the subject.

42. (withdrawn) The method of claim 41 further comprising administering to the subject a second dose of the agonist, wherein the second dose is administered as a function of the evaluated IL-10 parameter.

43. (withdrawn) The method of claim 41 wherein the agonist is selected from the group consisting of an IL-21 polypeptide, an agonistic anti-IL21R antibody and an antigen-binding fragment of an agonistic anti-IL21R antibody.

44. (withdrawn) The method of claim 43 wherein the agonist is an IL-21 polypeptide.

45. (withdrawn) The method of claim 44 wherein the subject is human, and the IL-21 polypeptide is a human IL-21 polypeptide.

46. (withdrawn) The method of claim 44 wherein the IL-21 polypeptide comprises SEQ ID NO:2.

47. (withdrawn) An article of manufacture comprising

(i) a container with one or more unit doses of a pharmaceutical composition comprising an IL-21 polypeptide; and

(ii) instructions for administering the unit doses to a subject that has, or is suspected of having, multiple sclerosis.

48. (withdrawn) The article of 47 wherein the instructions are provided on a label.

49. (withdrawn) The article of 48 wherein the label is affixed to an external surface of the container.